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RESEARCH

Association between triglyceride-glucose index and risk of acute kidney injury in patients with aneurysmal subarachnoid hemorrhage

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Abstract

Purpose This study aimed to investigate the association between the triglyceride-glucose (TyG) index and the risk of acute kidney injury (AKI) in patients with aneurysmal subarachnoid hemorrhage (aSAH).

Methods This retrospective cohort study included aSAH patients in West China Hospital. The TyG index was calculated as ln[fasting triglycerides (mg/dL) × fasting glucose (mg/dL)/2]. The primary outcome was AKI within 7 days of admission, and secondary outcomes included hospital, 90-day, and 180-day mortality. Multivariate logistic regression and Cox proportional hazards models were used to adjust for potential confounders. The association between the TyG index and AKI was also assessed with restricted cubic spline analysis. A predictive logistic model for AKI risk was developed and its performance was assessed using the area under the receiver operating characteristic curve, calibration correction curves, and decision curve analysis. Based on the optimal model, an online Shiny R application was developed.

Results A total of 3271 patients with aneurysmal subarachnoid hemorrhage were included. AKI occurred in 156 patients (4.7%), with the incidence significantly increasing across TyG index quartiles (Q1: 2.7%, Q4: 8.6%; P for trend < 0.001). Each 1-unit increase in TyG index was associated with an 90% higher odds of AKI (OR 1.90, 95% CI 1.48–2.45). Mortality rates also increased with higher TyG quartiles: hospital mortality (HR 1.30, 95% CI 1.05–1.62), 90-day mortality (HR 1.20, 95% CI 1.03–1.39), and 180-day mortality (HR 1.18, 95% CI 1.02–1.37). Kaplan–Meier analysis revealed reduced survival in higher TyG quartiles (Log-rank P < 0.001). Subgroup analyses confirmed consistent associations across demographics characteristics and treatment modalities. Incorporating the TyG index into risk models improves their discriminatory power and calibration. A Shiny application based on this model is freely accessible at (https://asahaki.shinyapps.io/asahaki/).

Conclusion The TyG index is an independent predictor of AKI and mortality in aSAH patients. Its incorporation into clinical assessment facilitates early risk stratification and individualized management.

Keywords TyG index · Subarachnoid hemorrhage · Acute kidney injury · Intracranial aneurysm · Mortality

Abbreviations

AKI	Acute kidney injury
AUC	Area under the curve
CTA	Computed tomography angiography
DSA	Digital subtraction angiography
IDI	Integrated discrimination improvement
NRI	Net reclassification improvement
ROC	Receiver operating characteristic curve
TyG	Triglyceride-glucose
aSAH	Aneurysmal subarachnoid hemorrhage

Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is a life-threatening cerebrovascular disorder caused by the rupture of an intracranial aneurysm, with an annual incidence of ≈6.1 per 100,000 person-years and a hospital mortality rate of approximately 20% [7, 30]. Despite advances in therapeutic strategies, aSAH remains associated with severe

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morbidity due to secondary events such as rebleeding, cerebral vasospasm, and systemic complications [13, 20]. Among these, acute kidney injury (AKI) has been recognized a critical complication, independently associated with increased mortality, prolonged hospitalization, and worsened functional outcomes [6, 33].

The pathogenesis of AKI in aSAH involves multifactorial mechanisms. Nephrotoxic effects of contrast agents used in computed tomography angiography, digital subtraction angiography and endovascular treatments, and hemodynamic instability caused by neurogenic shock and blood pressure fluctuations, are possible contributors [21, 26]. These factors can disrupt the endothelial glycocalyx, impair renal perfusion, and exacerbate kidney injury [3, 16]. These pathophysiological mechanisms underscore the need for effective strategies to identify and mitigate AKI risk in aSAH patients.

In recent years, metabolic dysfunction, particularly insulin resistance (IR), has been implicated in AKI development across various critical illnesses. The triglyceride-glucose (TyG) index, a simple and reliable surrogate marker of IR, has demonstrated predictive value in a variety of clinical contexts, including critically ill patients with AKI [17, 25]. Recent studies have reported its association with AKI in conditions such as traumatic brain injury, sepsis, and coronary interventions [8, 14, 29]. Furthermore, elevated TyG index levels have been linked to contrast-induced AKI (CI-AKI) in various populations undergoing contrast-enhanced imaging or interventions [14, 21, 29]. However, the relationship between the TyG index and AKI in patients with aneurysmal subarachnoid hemorrhage (aSAH) remains underexplored.

This study aims to investigate the association between the TyG index and AKI in aSAH patients in a high-volume tertiary center. We hypothesize that the TyG index may function as a clinically useful biomarker for early risk stratification, offering insights into metabolic mechanisms contributing to AKI and informing strategies to improve outcomes of aSAH patients.

Methods

Study design and population

This investigation was a single-center, observational, retrospective cohort analysis at West China Hospital, a tertiary academic medical institution. Adult patients admitted between November 2009 and July 2019 were included if subarachnoid hemorrhage was diagnosed by non-contrast computer tomography due to a ruptured aneurysm confirmed by computed tomography angiography (CTA) or digital subtraction angiography (DSA). Patients were excluded from the study if they: (1) had a history of trauma; (2) had arteriovenous malformations; (3) lacked data on fasting glucose or triglycerides; (4) had pre-existing kidney failure and/or serum creatinine > 4 mg/dl. This study was conducted in accordance with the Helsinki Declaration. Ethical approval for this study was granted by the Ethics Committee of West China Hospital (ethics code: 2023–869).

Management of subarachnoid hemorrhage

All patients received treatment in accordance with established international guidelines for the management of subarachnoid hemorrhage [5]. Nimodipine was initiated within 48 h of admission to mitigate the risk of vasospasm. Surgical clipping was prioritized as the first-line therapeutic approach at our institution, in preference to endovascular interventions. The application of nephroprotective measures was not governed by a standardized protocol. Vasopressor therapy was administered based on the individualized blood pressure needs of each patient.

Data collection

Demographic data and medical history were obtained from the electronic medical records. Venous blood samples were routinely collected by trained medical personnel on the morning following admission, after a minimum fasting period of 8 h. Concentrations of serum creatinine, fasting glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol were quantified using standardized biochemical assays in our center's clinical chemistry department. The estimated glomerular filtration rate (eGFR) was calculated using the 2009 CKD Epidemiology Collaboration (CKD-EPI) creatinine equation [22]. The TyG index was calculated using the following formula: ln [(fasting triglycerides (mg/dL) × fasting glucose (mg/dL))/2] [11]. Delayed ischemic neurological deficit (DIND) was defined as a delayed reduction in consciousness by at least two Glasgow Coma Scale (GCS) points, the emergence of a new focal neurological deficit, or evidence of cerebral ischemia on neuroimaging [14].

Endpoints and follow-up

Acute Kidney Injury (AKI) was diagnosed in accordance with the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines [18]. Specifically, AKI was identified if, within 7 days of admission, an increase in serum creatinine of ≥ 0.3 mg/dL and/or an increase to ≥ 1.5 times the baseline value. patients were considered to have developed AKI if their serum creatinine, initially below 4.0 mg/dL at admission, increased above 4.0 mg/dL during their hospitalization, or if they required hemodialysis at any point during their stay. Urine output criteria were not utilized in this study due to insufficient data.

Mortality data were obtained via the Household Registration Administration System, which operates on the foundation established by the Seventh National Census completed in 2020. In China, legal requirements stipulate that the death of a citizen must be reported to the household registration authority by the head of the household, relatives, dependents, or neighbors, who are also responsible for canceling the household registration within one month of the death [2]. Therefore, the death records in our system are accurate, resulting in an insignificant loss to follow-up in our study.

Statistical analysis and model evaluation

Continuous variables are presented as mean (standard deviation, SD) or the median with interquartile range (IQR), depending on the distribution of the data. Categorical variables are reported as frequencies and percentages (%). Differences between groups for categorical variables were assessed using the chi-squared test. For comparisons of continuous variables between two groups, the t-test or the Wilcoxon rank-sum test was applied, contingent on whether the data followed a normal distribution. When comparing continuous variables across more than two groups, a one-way analysis of variance (ANOVA) was performed, provided the data satisfied the assumptions of normality and homogeneity of variances. In cases where these assumptions were violated, the Kruskal–Wallis test was utilized as a non-parametric alternative. Missing values were assessed using Little's MCAR test with the "naniar" package in R [24], which indicated that the data were likely missing completely at random. Missing values were then imputed using the mean of the respective variable.

Logistic regression models were utilized to assess the association between the TyG index and binary outcomes, while Cox proportional hazards regression models were applied for time-to-event outcomes. The TyG index was analyzed both as a continuous variable and as a categorical variable divided into quartiles. Confounding variables were selected based on prior literature and included in the multivariable models if their p-values were less than 0.05 in univariable analysis. Three logistic regression models were developed: Model 1, which was unadjusted; Model 2, which adjusted for demographic factors (age, sex) and aneurysm characteristics (location, size, WFNS grade); and Model 3, which additionally accounted for medical history and aneurysm treatment. Potential nonlinear relationships were examined using restricted cubic splines (RCS) with four knots, and the significance of nonlinearity was assessed with the log-likelihood ratio test. Subgroup analyses were performed based on the following variables: age (≥ 60 years), sex, smoking status, alcohol consumption, hypertension, diabetes, coronary artery disease, chronic renal failure, aneurysm location (anterior vs. posterior circulation), aneurysm size (≥ 1 cm), and aneurysm management. Interactions between the TyG index and these factors were evaluated through likelihood ratio tests. Kaplan–Meier survival curves were constructed to assess the relationship between the TyG index and patient mortality, with comparisons conducted using the log-rank test. Additionally, mediation analysis was performed using the'mediation'package in R to assess the role of AKI in the relationship between the TyG index and 90-day mortality [15, 34, 35]. A logistic regression model was developed to predict AKI risk in aSAH patients. Key clinical variables, including demographic and medical factors, were incorporated into the model. Its performance was evaluated using the area under the receiver operating characteristic curve, the Hosmer–Lemeshow test, calibration curve, and decision curve analysis to assess prediction accuracy and clinical applicability. The clinical utility of adding the TyG index to the existing risk factors for predicting AKI in aSAH patients was assessed using the integrated discrimination improvement (IDI) and net reclassification improvement (NRI) indices [36]. Considering the potential impact of early mortality on the onset of AKI during hospitalization, a sensitivity analysis was performed to further assess the robustness of the results. Specifically, patients who died within 7 days of admission were excluded to evaluate the association between the TyG index and AKI more accurately. All statistical analyses were conducted using R software, version 4.3.0. A p-value < 0.05 was considered statistically significant.

Results

Study population characteristics

The final study cohort included 3271 patients, stratified into four quartiles based on the TyG index. The detailed patient selection process is outlined in Fig. 1. The mean age of the cohort was 55.11 years (SD 11.93), and 65.1% of the participants were female. Patients in higher TyG quartiles tended to have an increased prevalence of hypertension, rising from 17.2% in the first quartile (Q1) to 30.1% in the fourth quartile (Q4) ($P < 0.001$). Similarly, the proportion of patients with higher WFNS grades (IV–V) increased significantly from 18.1% in Q1 to 31.8% in Q4 ($P < 0.001$). No significant differences were observed in smoking status, alcohol consumption, comorbidities such as diabetes and coronary heart disease, aneurysm location, or aneurysm management strategies across TyG quartiles ($P > 0.05$ for all). Laboratory findings demonstrated significant differences among quartiles. Higher TyG quartiles were associated with increased fasting blood glucose, triglyceride levels, and low-density lipoprotein cholesterol, while estimated glomerular filtration rate decreased significantly across the quartiles (Table 1).

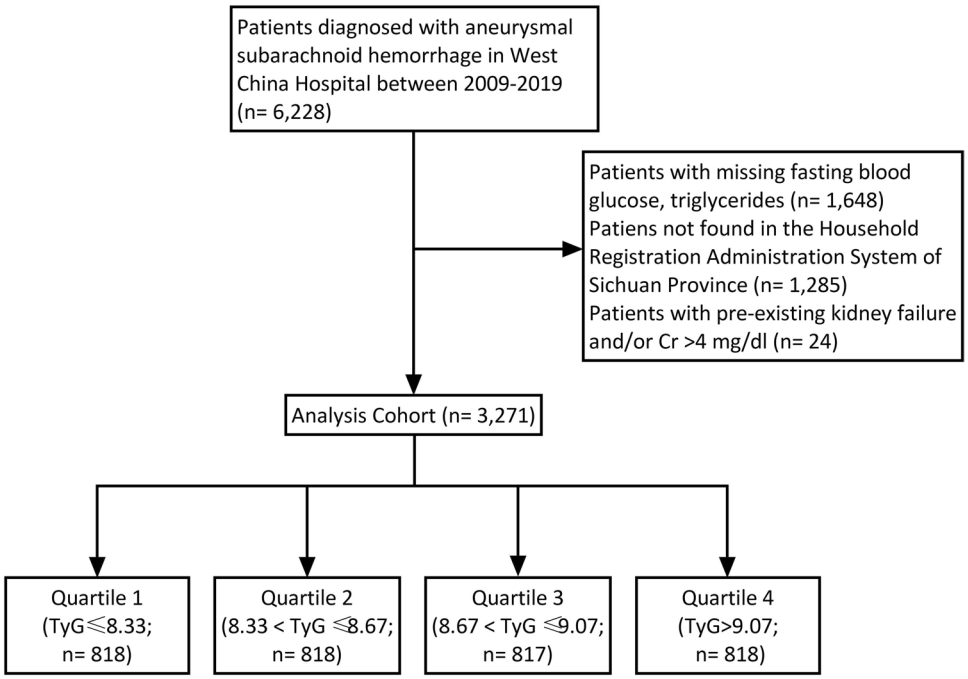

Fig. 1 Flowchart of patient selection. Cr, serum creatinine

Table S1 presents the baseline characteristics of the study population stratified by the presence or absence of AKI. Patients in the AKI group were older, and had a higher prevalence of comorbidities, including hypertension and diabetes. Similarly, a greater proportion of patients in the AKI group had higher WFNS grades. Laboratory findings revealed that patients in the AKI group had higher TyG index values compared to the non-AKI group.

Associations between TyG index and AKI

Of the 3271 patients included in the study, 156 (4.7%) developed acute kidney injury within 7 days of admission. The incidence of AKI increased significantly across TyG index quartiles, with a higher prevalence observed in the upper quartiles (Q1: 2.7%, Q2: 2.7%, Q3: 5.1%, Q4: 8.6%; P for trend <0.001). In the unadjusted logistic regression model (Model 1), patients in the quartile 4 had more than a threefold higher risk of AKI compared to those in the quartile 1 (OR 3.39, 95% CI: 2.08–5.52, $P<0.001$). After sequential adjustment for potential confounding variables (Models 2 and 3), the association between the TyG index and AKI risk remained statistically significant. In the fully adjusted model (Model 3), each 1-unit increase in the TyG index was associated with an 90% higher odds of AKI (OR 1.90, 95% CI: 1.48–2.45, $P<0.001$). The association between TyG quartiles and AKI risk also demonstrated a significant trend from Q1 to Q4 across all models ($P<0.001$) (Table 2, Table S2).

Multivariable restricted cubic spline analysis, with full adjustment for clinically relevant covariates, demonstrated a linear relationship between the TyG index and AKI risk ($P=0.42$). AKI risk increased consistently with higher TyG index values, with no evidence of a non-linear association (Fig. 2).

Associations between TyG index and mortality

The overall mortality rates in the study population were 5.50% for hospital mortality, 11.59% for 90-day mortality, and 13.08% for 180-day mortality. When categorized into quartiles, patients in Q4 had significantly higher risks of hospital mortality (HR 1.81, 95% CI 1.13–2.92, $P=0.014$), 90-day mortality (HR 1.53, 95% CI 1.09–2.15, $P=0.014$), and 180-day mortality (HR 1.46, 95% CI 1.06–2.03, $P=0.022$) compared to those in Q1. A significant trend across quartiles was observed for all endpoints (P for trend $=0.02$). When analyzed as a continuous variable, each 1-unit increase in the TyG index was associated with a 30% higher risk of hospital mortality (HR 1.30, 95% CI 1.05–1.62, $P=0.01$), a 20% higher risk of 90-day mortality (HR 1.20, 95% CI 1.03–1.39, $P=0.02$), and an 18% higher risk of 180-day mortality (HR 1.18, 95% CI 1.02–1.36, $P=0.02$) (Table 3, Table S3).

Kaplan–Meier survival curves demonstrated decreasing survival probabilities with increasing TyG index quartiles. Patients in Q4 exhibited the lowest survival probabilities throughout the follow-up period, with a noticeable divergence in survival curves over time. The Log-rank test confirmed significant differences in survival between quartiles ($P<0.001$) (Fig. 3). The mediation analysis revealed that 21.2% of the observed association between the TyG index and hospital mortality, 19.7% of the association with 90-day

Table 1 Baseline characteristics of patients with quartile TyG index

Characteristics	Total ($n = 3271$)	Quartile 1 ($n = 818$)	Quartile 2 ($n = 818$)	Quartile 3 ($n = 817$)	Quartile 4 ($n = 818$)	p
Age, mean (SD)	55.11 (11.93)	53.67 (13.15)	55.25 (11.77)	55.51 (11.22)	56.01 (11.36)	0.001
Female, *n* (%)	2129 (65.1)	524 (64.1)	524 (64.1)	536 (65.6)	545 (66.6)	0.635
Smoking status, *n* (%)						0.720
Current smoker	140 (4.3)	32 (3.9)	34 (4.2)	40 (4.9)	34 (4.2)	
Previous smoker	656 (20.1)	165 (20.2)	163 (19.9)	150 (18.4)	178 (21.8)	
Never	2475 (75.7)	621 (75.9)	621 (75.9)	627 (76.7)	606 (74.1)	
Drinking, *n* (%)	643 (19.7)	159 (19.4)	159 (19.4)	153 (18.7)	172 (21.0)	0.724
Medical history, *n* (%)						
Hypertension	808 (24.7)	141 (17.2)	185 (22.6)	236 (28.9)	246 (30.1)	< 0.001
Diabetes	183 (5.6)	19 (2.3)	28 (3.4)	33 (4.0)	103 (12.6)	< 0.001
Coronary heart disease	82 (2.5)	24 (2.9)	18 (2.2)	20 (2.4)	20 (2.4)	0.814
Chronic obstructive pulmonary disease	233 (7.1)	61 (7.5)	59 (7.2)	58 (7.1)	55 (6.7)	0.951
WFNS, *n* (%)						< 0.001
I	1895 (57.9)	513 (62.7)	507 (62.0)	471 (57.6)	404 (49.4)	
II	542 (16.6)	140 (17.1)	140 (17.1)	135 (16.5)	127 (15.5)	
III	88 (2.7)	17 (2.1)	21 (2.6)	23 (2.8)	27 (3.3)	
IV	333 (10.2)	81 (9.9)	75 (9.2)	86 (10.5)	91 (11.1)	
V	413 (12.6)	67 (8.2)	75 (9.2)	102 (12.5)	169 (20.7)	
Aneurysm characteristics						
Anterior location, *n* (%)	2669 (81.6)	666 (81.4)	672 (82.2)	650 (79.6)	681 (83.3)	0.269
Size of aneurysm, cm, mean (SD)	0.76 (0.69)	0.77 (0.76)	0.77 (0.67)	0.74 (0.61)	0.78 (0.71)	0.827
Management of aneurysm, *n* (%)						0.711
No treatment	663 (20.3)	171 (20.9)	165 (20.2)	156 (19.1)	171 (20.9)	
Clip	2195 (67.1)	549 (67.1)	546 (66.7)	546 (66.8)	554 (67.7)	
Coil	413 (12.6)	98 (12.0)	107 (13.1)	115 (14.1)	93 (11.4)	
External ventricular drain, *n* (%)	70 (2.1)	14 (1.7)	10 (1.2)	24 (2.9)	22 (2.7)	0.053
DIND, *n* (%)	616 (18.8)	138 (16.9)	163 (19.9)	159 (19.5)	156 (19.1)	0.401
No. of cerebral angiograms, mean (SD)	2.31 (1.00)	2.26 (1.03)	2.32 (0.98)	2.32 (0.99)	2.34 (0.98)	0.438
Antibiotics use, *n* (%)	1206 (36.9)	293 (35.8)	266 (32.5)	305 (37.3)	342 (41.8)	0.001
Laboratory results, mean (SD)						
FBG, mg/dL	125.69 (43.60)	105.61 (24.06)	114.77 (27.06)	124.10 (32.85)	158.26 (60.26)	< 0.001
TG, mg/dL	122.09 (94.89)	62.71 (16.98)	90.46 (20.55)	119.92 (28.83)	215.28 (145.83)	< 0.001
TC, mmol/L	4.40 (1.00)	4.01 (0.88)	4.32 (0.95)	4.49 (0.96)	4.77 (1.05)	< 0.001
HDL-C, mmol/L	1.38 (0.44)	1.53 (0.44)	1.43 (0.44)	1.35 (0.42)	1.23 (0.41)	< 0.001
LDL-C, mmol/L	2.52 (0.81)	2.20 (0.71)	2.49 (0.79)	2.63 (0.79)	2.75 (0.86)	< 0.001
Serum creatinine, mg/dL	0.70 (0.25)	0.66 (0.20)	0.67 (0.20)	0.72 (0.26)	0.76 (0.30)	< 0.001
eGFR, mL/min/1.73 m^2	99.43 (18.80)	103.92 (17.91)	101.62 (17.66)	97.81 (18.12)	94.34 (20.03)	< 0.001

SD standard deviation, *TyG* Triglyceride glucose index, *DIND* delayed ischemic neurological deficit; No. of cerebral angiograms, total number of computed tomography angiography (CTA) and digital subtraction angiography (DSA) procedures combined; *FBG* fasting blood glucose, *TG* triglyceride, *TC* total cholesterol, *HDL-C* high-density lipoprotein, *LDL-C* low-density lipoprotein, *eGFR* estimated glomerular filtration rate

mortality, and 19.4% of the association with 180-day mortality were mediated through the occurrence of acute kidney injury ($P < 0.001$) (Figure S1).

Subgroup analyses

The association between higher TyG index values (Q3–Q4)

Table 2 Association between TyG index and AKI

TyG index	Number of AKI (%)	Model 1		Model 2		Model 3	
		OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Continuous	156(4.7%)	2.07 (1.66–2.57)	**< 0.001**	2.06 (1.62–2.61)	**< 0.001**	1.90 (1.48–2.45)	**< 0.001**
Q1 (≤ 8.33; *N* = 818)	22 (2.7%)	1	Ref	1	Ref	1	Ref
Q2 (8.33 < TyG ≤ 8.67; *N* = 818)	22 (2.7%)	1.00 (0.55–1.82)	1	0.96 (0.52–1.76)	0.884	1.01 (0.54–1.86)	0.985
Q3 (8.67 < TyG ≤ 9.07; *N* = 817)	42 (5.1%)	1.96 (1.16–3.32)	**0.012**	1.85 (1.08–3.16)	**0.002**	1.75 (1.01–3.01)	0.045
Q4 (> 9.07; *N* = 818)	70 (8.6%)	3.39 (2.08–5.52)	**< 0.001**	2.96 (1.78–4.90)	**< 0.001**	2.70 (1.60–4.55)	**< 0.001**
P for trend			**< 0.001**		**< 0.001**		**< 0.001**

Model 1: unadjusted; Model 2: adjusted for age, sex, aneurysm location, aneurysm size, WFNS grade; Model 3: adjusted for age, sex, smoking, hypertension, diabetes, aneurysm location, aneurysm size, WFNS grade, management of aneurysm, antibiotics use. *AKI* acute kidney injury, *TyG index* triglyceride-glucose index, *OR* odds ratio, *CI* confidence interval

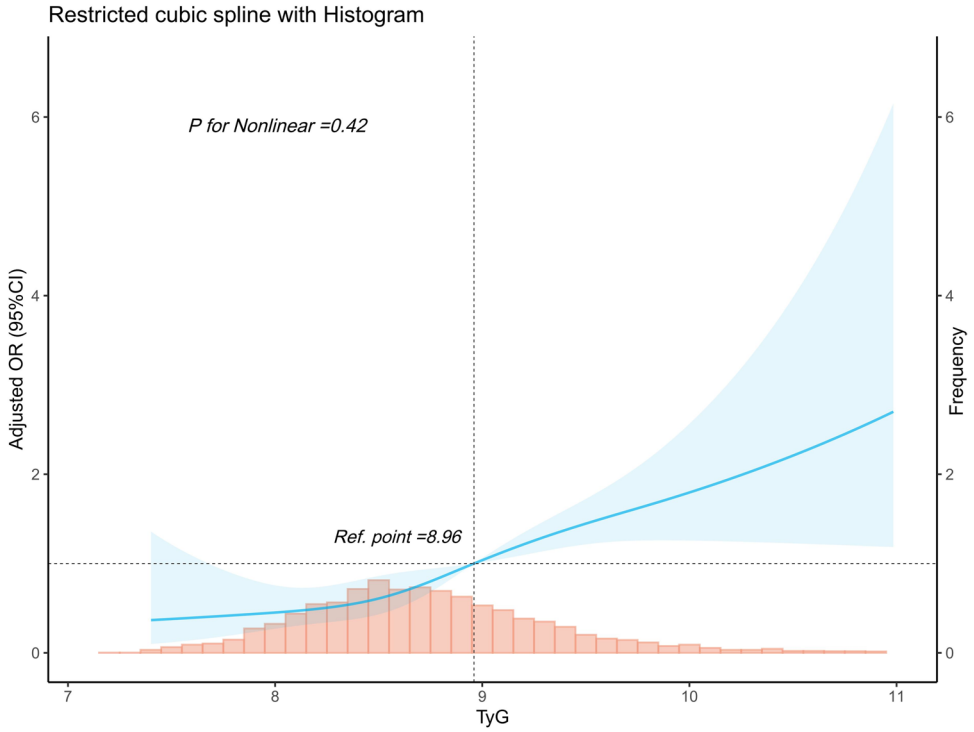

Fig. 2 Restricted cubic splines curve of TyG index with AKI in patients with aneurysmal subarachnoid hemorrhage

Table 3 Association between TyG index and mortality

TyG index	Hospital mortality		90-day mortality		180-day mortality	
	n (%)	HR (95% CI), *P*	*n* (%)	HR (95% CI), *P*	*n* (%)	HR (95% CI), *P*
Continuous		1.30 (1.05–1.62), **0.01**		1.20 (1.03–1.39), **0.02**		1.18 (1.02–1.37), **0.02**
Q1 (≤ 8.33; *N* = 818)	30 (3.7%)	Ref	74 (9.0%)	Ref	83 (10.1%)	Ref
Q2 (8.33 < TyG ≤ 8.67; *N* = 818)	39 (4.8%)	1.31 (0.78–2.19), 0.314	89 (10.9%)	1.22 (0.85–1.73), 0.277	102 (12.5%)	1.26 (0.90–1.76), 0.174
Q3 (8.67 < TyG ≤ 9.07; *N* = 817)	34 (4.2%)	0.94 (0.55–1.61), 0.831	72 (8.8%)	0.80 (0.55–1.17), 0.252	88 (10.8%)	0.91 (0.64–1.28), 0.576
Q4 (> 9.07; *N* = 818)	77 (9.4%)	**1.81 (1.13–2.92), 0.014**	144 (17.6%)	**1.53 (1.09–2.15), 0.014**	155 (18.9%)	**1.46 (1.06–2.03), 0.022**
P for trend		**0.01**		**0.02**		**0.02**

Adjusted for age, sex, smoking, hypertension, diabetes, aneurysm location, aneurysm size, WFNS grade, management of aneurysm, antibiotics use. *TyG index* triglyceride-glucose index, *HR* hazard ratio, *CI* confidence interval

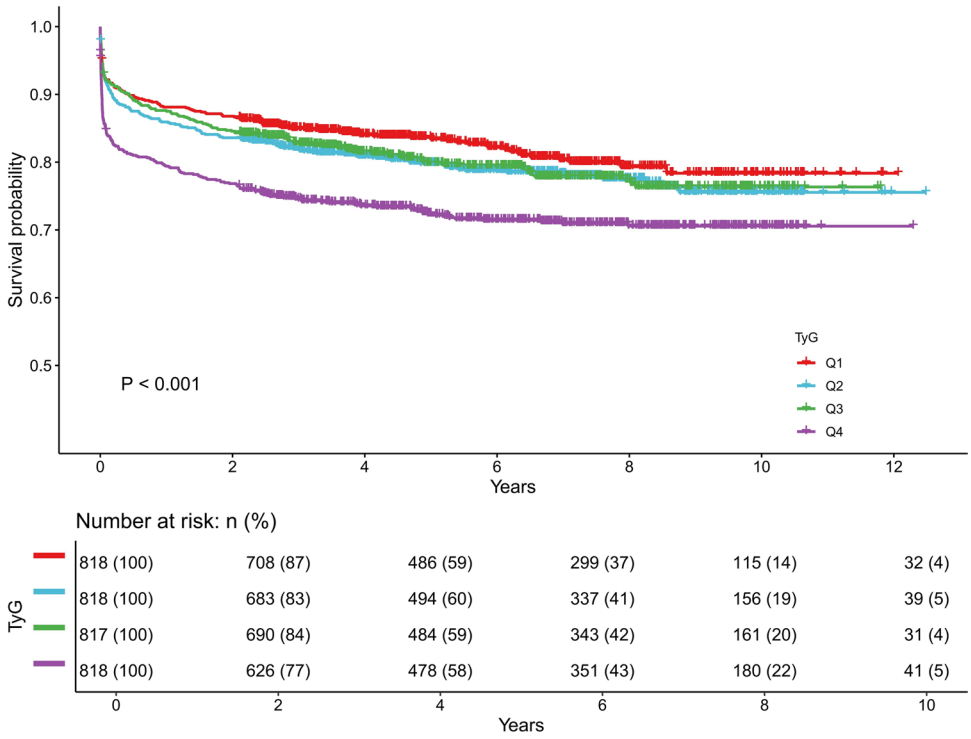

Fig. 3 Kaplan–Meier survival estimates of long-term mortality in patients with TyG index quartiles

and adverse outcomes remained consistent across all evaluated subgroups, including sex, age, smoking status, diabetes, hypertension, and other comorbidities. The observed association was more pronounced in certain subgroups, such as male patients (OR 2.31, 95% CI 1.41–3.76), patients aged > 60 years (OR 2.10, 95% CI 1.19–3.69), and those with WFNS grades IV–V (OR 3.12, 95% CI 1.72–5.66). When comparing treatment modalities, higher TyG index values were associated with a greater risk of AKI in patients receiving conservative management (OR 2.77, 95% CI 1.35–5.70) compared to those undergoing active interventions such as coil embolization or clipping (OR 2.05, 95% CI 1.32–3.17). Additionally, no significant interactions were detected across subgroups (Fig. 4).

Predictive ability and incremental effect of TyG index in risk stratification

To assess the predictive ability of the TyG index, we calculated the area under the receiver operating characteristic (ROC) curve (AUC) for its ability to predict AKI and mortality. The results demonstrated that, in patients with subarachnoid hemorrhage, the AUC of the TyG index to predict AKI was higher than 0.6 (IQR: 0.638 [0.594, 0.681]; numeric: 0.651 [0.606, 0.700]). The AUC values for TyG in predicting hospital mortality, 90-day mortality, and 180-day mortality were 0.605, 0.573, and 0.567 respectively (Fig. S2).

We compared the predictive ability of the basic risk model versus the model with TyG for AKI. The inclusion of the TyG index improved the AUC from 0.778 to 0.796, indicating an enhanced predictive accuracy for AKI. Decision curve analysis showed a higher net clinical benefit for the model incorporating the TyG index compared to the basic model. Furthermore, the calibration curve demonstrated good agreement between predicted and observed outcomes, with the TyG-enhanced model showing a closer fit to the ideal curve (Fig. 5). The inclusion of the TyG index also led to significant improvements in the predictive ability of the model, as evidenced by positive NRI and IDI values ($P < 0.01$) for AKI (Table 4). A R Shiny web tool based on a logistic regression model incorporating the TyG index was developed to predict AKI risk in patients with aSAH. This web application can be accessed at https://asahaki.shinyapps.io/asahaki/, where users can input clinical and laboratory data to calculate the likelihood of developing AKI within 7 days of admission (Fig. S3).

Sensitivity analysis

After excluding patients who died within 7 days of admission, the association between the TyG index and the incidence of AKI remained stable (Table S4, Table S5, Table S6, and Fig. S4). These findings aligned with the primary results that included all patients.

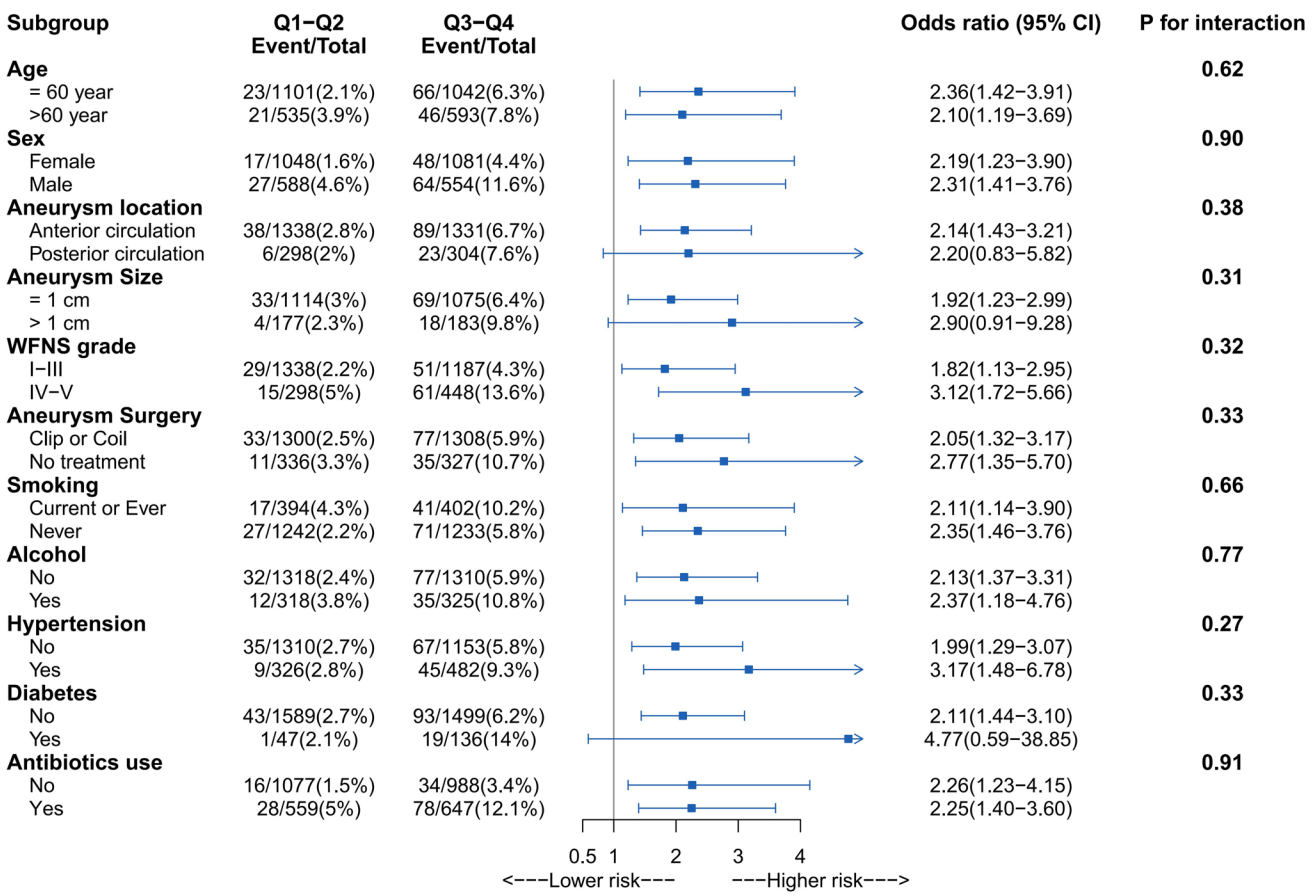

Fig. 4 Subgroup analysis of associations between TyG index and AKI. The odds ratios (ORs) for the risk of AKI in each subgroup were calculated using a logistic regression model, adjusting for age, sex, smoking status, hypertension, diabetes, aneurysm location, aneurysm size, WFNS grade, management of aneurysm, and antibiotics use, except when these variables were used as stratification factors for subgroup analysis. The TyG index was categorized by combining the first and second quartiles into one group and the third and fourth quartiles into another group. The risk of AKI was then calculated for the higher TyG group relative to the lower TyG group. Interaction terms between the TyG index and each subgroup were included in the model, and the corresponding P-values for these interactions are displayed in the figure

Discussion

This study is the first to comprehensively examine the association between the triglyceride-glucose (TyG) index and acute kidney injury (AKI) in patients with aneurysmal subarachnoid hemorrhage (aSAH). Our findings indicate that higher TyG quartiles are independently linked to an increased risk of AKI and elevated mortality rates at hospital discharge, as well as at 90 and 180 days post-admission. A linear relationship was identified between the TyG index and AKI risk, and survival probabilities decreasing as TyG quartiles increased. These results highlight the significance of metabolic factors, particularly the TyG index, in predicting AKI and mortality in aSAH patients, extending beyond traditional clinical risk factors.

Previous studies have demonstrated that the TyG index is significantly associated with an increased risk of cardiovascular diseases, chronic kidney disease, and metabolic syndrome, highlighting its potential as a marker for metabolic dysregulation [4, 9, 28]. In cerebrovascular diseases, the TyG index has been shown to predict all-cause mortality and recurrence among ischemic stroke patients [41], as well as early neurological deterioration in acute ischemic stroke [40]. Furthermore, in critically ill patients with hemorrhagic stroke, it has been identified as an independent predictor of both in-hospital and long-term mortality [23, 38]. Building on this foundation, our study demonstrates the TyG index's utility in predicting acute kidney injury and mortality in aSAH patients. By analyzing a larger cohort that includes both ICU and non-ICU patients, we provide comprehensive evidence for the TyG index as a valuable tool for risk stratification and early intervention.

Previous studies have explored acute kidney injury (AKI) in patients with aneurysmal subarachnoid hemorrhage (aSAH), with most focusing on clinical characteristics and renal-related markers such as sex, uric acid levels,

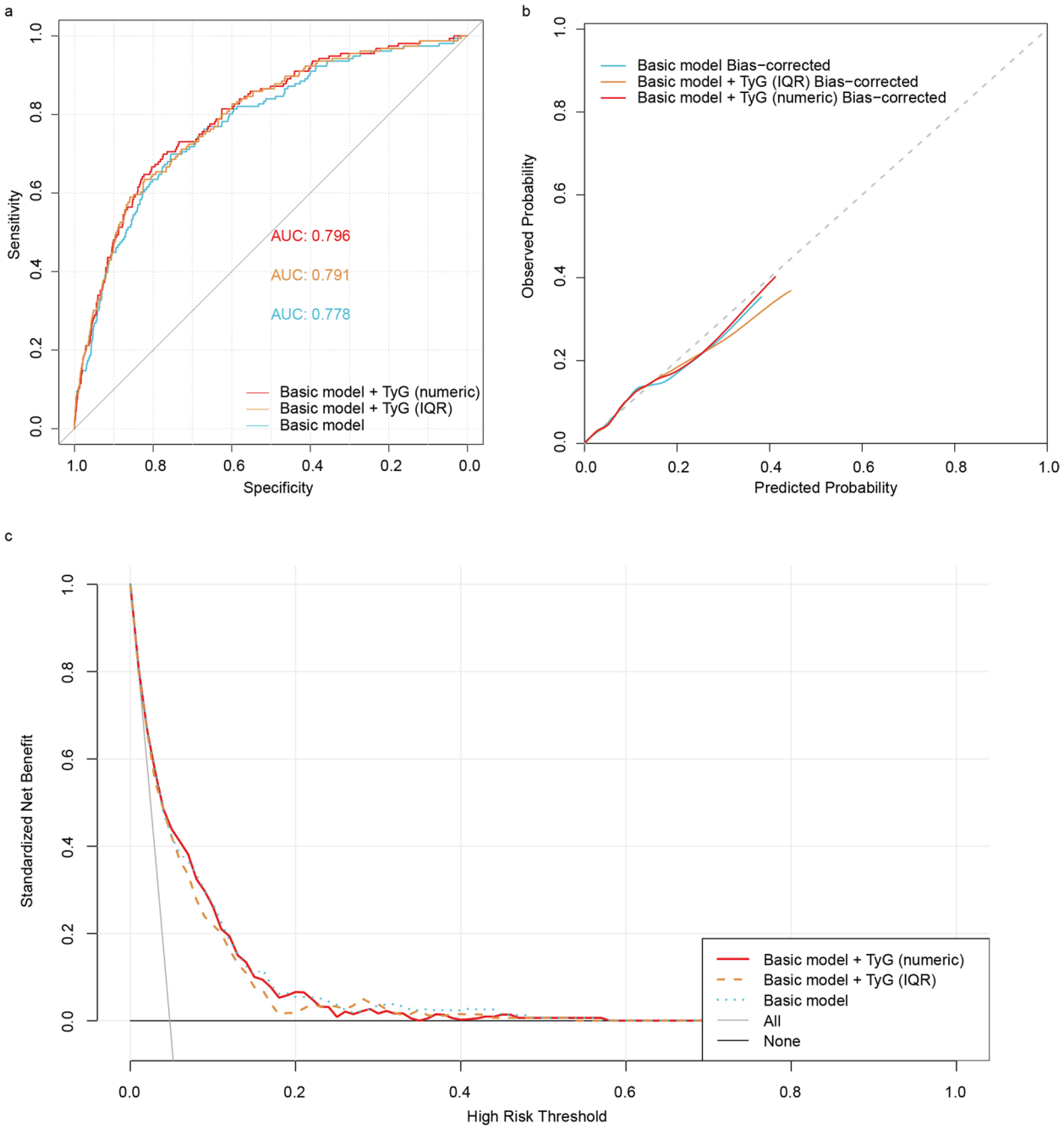

Fig. 5 Comparison of predictive performance for AKI using the basic model and TyG-enhanced model. **a**. AUC comparison: The inclusion of the TyG index improved the AUC from 0.754 to 0.771, enhancing predictive accuracy for AKI. **b**. Decision curve analysis: The TyG-enhanced model demonstrated a higher net clinical benefit than the basic model. **c**. Calibration curve: The TyG-enhanced model showed better calibration, with predictions more closely aligned to the ideal curve

hyperchloremia, and hypernatremia [10, 19, 31, 39]. For instance, Fukuda et al. identified elevated uric acid levels as an independent predictor of AKI in aSAH patients [10]. Similarly, research by Kumar et al. highlighted hypernatremia as a significant risk factor for AKI, with increased serum sodium exposure, often associated with hypertonic saline therapy, linked to a higher risk of AKI development [19]. Our study demonstrates that the triglyceride-glucose index, a reliable marker of IR, is significantly associated with the development of AKI in aSAH patients. Furthermore, incorporating the TyG index into risk models enhances both their discriminatory power and calibration, reinforcing the importance of insulin resistance in AKI risk stratification for this population.

Table 4 The incremental effect of the TyG index

Representation of TyG Index in the Model	AUC [95% CI]	IDI [95% CI] (+ TyG)	P-value	NRI [95% CI] (+ TyG)	P-value
Continuous Variable	0.796 (0.760–0.832)	0.011 (0.004–0.0184)	**0.0026**	0.393 (0.224–0.553)	**< 0.001**
Quartile Variable	0.792 (0.755–0.828)	0.010 (0.004–0.0165)	**0.0014**	0.386 (0.229–0.536)	**< 0.001**

Adjusted for age, sex, smoking, hypertension, diabetes, aneurysm location, aneurysm size, management of aneurysm, WFNS grade, antibiotics use. *AKI* acute kidney injury, *TyG index* triglyceride-glucose index, *AUC* area under the curve, *CI* confidence interval, *IDI* integrated discrimination improvement, *NRI* net reclassification improvement

The observed association between higher TyG index and AKI risk can be explained by several mechanisms, including metabolic dysregulation, hemodynamic instability, and oxidative stress. Insulin resistance, reflected by the TyG index, increases glomerular hydrostatic pressure, impairing filtration and causing hyperfiltration [32]. It also activates the RAAS, elevating angiotensin II and aldosterone, leading to renal vasoconstriction and decreased perfusion [27]. In aSAH, local hemodynamic instability and vasospasm exacerbates these effects, worsening AKI and increasing mortality risk [1, 6, 37]. Oxidative stress may be another mechanism linking the TyG index to AKI. Insulin resistance enhances the formation of reactive oxygen species (ROS), which can induce renal parenchymal hypoxia and direct tubular and vascular endothelial injury, contributing to kidney injury [12]. Future research is needed to establish causality between the TyG index and AKI and mortality in aSAH patients, and to explore the mechanisms underlying these associations.

Subgroup analyses demonstrated that the association between the TyG index and adverse outcomes, including AKI and mortality, was consistent across various patient subgroups, such as sex, age, smoking status, comorbidities, and treatment modalities (coiling, clipping, or conservative management). This robustness highlights the potential generalizability of the TyG index as a prognostic marker in diverse aSAH populations.

Our findings suggest that the TyG index could serve as a simple, cost-effective biomarker for early risk prediction in aSAH patients. Integrating the TyG index into routine clinical assessments could facilitate the early identification of high-risk individuals, enabling timely interventions. Proactive management strategies, such as optimizing glucose and lipid control, may help reduce the risk of AKI and improve survival outcomes. Additionally, we have developed an online platform (https://asahaki.shinyapps.io/asahaki/) that incorporates the TyG index to assist clinicians in risk stratification and decision-making. This platform aims to support real-time clinical evaluations and facilitate personalized treatment plans for aSAH patients.

Strengths and limitations

The present study has several strengths, including a large sample size, robust statistical adjustments for confounders, and comprehensive evaluation of both short- and long-term outcomes. However, despite these valuable insights, it is important to recognize several limitations. First, this is an observational study, and although we adjusted for a range of potential confounders, residual confounding cannot be ruled out. Second, the unavailability of detailed information regarding the administration of diabetes and lipid-lowering medications obscures the assessment of their effects. Third, due to the retrospective nature of this study, we were unable to include chronic hydrocephalus in the analysis of long-term mortality. Fourth, although our study included a large cohort of patients, reliance on data from a single center may limit the generalizability of the findings. Therefore, there is a need for prospective, multicenter studies to confirm the reliability of the findings and further investigate the efficacy of targeted interventions such as blood glucose or triglyceride reduction in improving patient outcomes.

Conclusion

This study identified the triglyceride-glucose (TyG) index as an independent predictor of acute kidney injury (AKI) and mortality in patients with aneurysmal subarachnoid hemorrhage (aSAH). Our findings suggest that incorporating the TyG index into clinical practice could enhance risk stratification and facilitate the early identification of high-risk patients, thereby supporting the development of personalized management strategies. Further prospective studies are needed to validate these results and investigate the underlying mechanisms.

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Author contributions Conceptualization: Xingyu Qiu, Yu Zhang, Jialing He, Renjie Zhang; Methodology: Xingyu Qiu, Dingke Wen, Xing Wang; Formal analysis and investigation: Xingyu Qiu, Yu Zhang,

Jialing He, Renjie Zhang; Writing—original draft preparation: Xingyu Qiu; Writing—review and editing: Xingyu Qiu, Yu Zhang, Jialing He, Renjie Zhang, Dingke Wen, Xing Wang, Fang Fang and Lu Ma; Funding acquisition: Dingke Wen and Lu Ma; Supervision: Chao You, Fang Fang and Lu Ma. All authors read and approved the final manuscript.

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Data availability Original data supporting the findings of this study is available from the corresponding author upon reasonable request.

Declarations

Ethical Approval The institutional review board of the ethics committee of West China Hospital approved the study (ethics code: 2023–869).

Consent to participate Informed consent to participate was waived by the institutional review board of the ethics committee of West China Hospital due to the minimal risk posed to patients.

Consent for publication Not applicable, as no identifying information of individual participants are included in this manuscript.

Competing interests The authors declare no competing interests.

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